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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/720,600	11/24/2003	Paul S. Changelian	PC25530A	5009

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
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GROTON, CT 06340

EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 08/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/720,600	CHANGELIAN, PAUL S.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/9/04, 3/19/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-15 are pending.

Information Disclosure Statement

References cited in the Information Disclosure Statements filed on 1/9/2004 & 3/19/2004, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Any claim not specifically rejected is rejected, as it is a dependent claim on a rejected claim.

1. Recitation of " including" in claims 1, 14 and 15, renders these claims indefinite as the transitional term "including" is open and implies more than what is being positively recited therein. See MPEP 2111.03 which states under transitional phrases The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., Genentech, Inc. v. Chiron Corp., 112 F.3d 495,501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir.

1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts").

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating acute organ transplant rejection, does not reasonably provide enablement for preventing acute organ transplant rejection embraced in the instant invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Method claims 1-14 and pharmaceutical composition claim 15 with intended uses are not adequately enabled for preventing acute organ transplant rejection recited therein. The instant method of use claims 1-14 and pharmaceutical composition claim 15 with intended use are drawn to "a method of treating or preventing acute organ transplant rejection for which there is no enabling disclosure in the specication.

The scope of the claims includes not only treatment but also prevention of a said disorder, which is not adequately enabled solely based on the activity of the compounds as tyrosine kinase or Janus kinase 3 inhibitors provided in the specification at pages 25-26. "To prevent" actually means to anticipate or counter in advance, to keep from happening etc. (as per Websters II Dictionary) and there is no disclosure as to how one

skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein.

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288 . Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method preventing the said diseases solely based on the inhibitory activity disclosed for the compounds. The state of the art at the time of instant invention is indicative of the requirement for undue experimentation. See Shouda et al., The Journal of Clinical Investigation 108(12): 1781-1788, 1998 , Aringer et al., Life Sciences 64(24): 2173-2186, 1999 and Traxler et al. Ex. Opin. Ther. Patents 7(6): 571-588, 1997.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or

lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Use of the compounds for in preventing acute organ transplant rejection that require protein tyrosine kinase or Janus kinase inhibitory activity.

2) The state of the prior art: A recent publications expressed that the protein tyrosine kinase or Janus kinase inhibition effects are unpredictable and are still exploratory.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for preventing acute organ transplant rejection embraced for the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show preventing psoriasis, organ transplant rejection and rheumatoid arthritis embraced in the instant claims and the state of the art is that the effects of protein kinase inhibitors are unpredictable.

6) The breadth of the claims: The instant claims embrace preventing acute organ transplant rejection due to protein tyrosine kinase or Janus kinase.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards preventing acute organ transplant rejection embraced in the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was 'filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 15 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over compound claims 1-4 of U.S. Patent No. 6,627,754. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pharmaceutical composition embraced in the instant claim would be obvious over the compound claims 1-4 of US 6,627,754. Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds using the teachings of claims 1-4 of US 6,627,754 and expect resulting compounds and their composition to possess the uses taught by the art.

Claims 15 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over compound claims 1-4 of U.S. Patent No. 6,890,929. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pharmaceutical composition embraced in the

instant claim would be obvious over the compound claims 1-4 of US 6,890,929. Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds using the teachings of claims 1-4 of US 6,890,929 and expect resulting compounds and their composition to possess the uses taught by the art.

Claims 1-15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4 and 5 of U.S. Patent No. 6,956,041. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter embraced in the instant claim is also embraced in the mode of action of the claims 4 and 5 of US 6,956,041. In this regard applicants attention to drawn to the court decision, wherein the court held that double patenting applies between a mode of action and the treatment of disease if one of ordinary skill in the art would know of the connection between the two. See Lilly vs. Barr, 58 USPQ2d 1869, at 1879. Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds using the teachings of claims 4 and 5 and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Claims 1-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 27-48 of copending Application No. 11/211,217. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treating various diseases embraced in the instant claims are also embraced in the claims 27-48 of the

copending application 11/211,217. Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds using the teachings of 11/211,217 and expect resulting compounds to possess the use for treating acute organ transplant rejection.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 7, 8, 10, 12-16 and 19 of copending Application No. 11/064,873. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treating various diseases embraced in the instant claims are also embraced in the claims 7, 8, 10, 12-16 and 19 of the copending application 11/064,873. Note claims 9 and 11 are included as they relate to mode of action, namely inhibiting tyrosine kinase. In this regard applicants' attention to drawn to the court decision, wherein the court held that double patenting applies between a mode of action and the treatment of disease if one of ordinary skill in the art would know of the connection between the two. See Lilly vs. Barr, 58 USPQ2d 1869, at 1879. Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds using the teachings of 11/211,217 and expect resulting compounds and their pharmaceutical compositions to possess the use for treating acute organ transplant rejection.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 14 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 1. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claim 1 and claim 14 appears to embrace the same subject matter with same scope. It is not clear what is the difference between the tow claims.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you

have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

Venkataraman Balasubramanian

8/23/2005